REPORT ON TECHNICAL CONSULTANCY AT FEDERAL VACCINE PRODUCTION LABORATORIES/ YELLOW FEVER VACCINE PRODUCTION, YABA, LAGOS, NIGERIA.

Ref: Yellow Fever (Nigéria) T-87-073
Period of consultancy: October 4 - 19, 1987
Place: Federal Vaccine Production Laboratories, Yaba, Lagos.

1 - Objectives of consultancy:

- evaluation of local Yellow Fever/Yellow Fever Vaccine Production.
- discussion on details of vaccine production.
- discussion on the requirements of material and training in order to upgrade the YF facility.
- assistance to the Federal Vaccine Production Laboratories (FVPL) in the preparation of proposal of a Project for modernization and upgrading of YF Vaccine Production, Yaba, for IDRC submission.

2 - Contacts made during the visit:

- Professor Ransone - Kuti, Federal Minister of Health, Federal Ministry of Health, Ikoyi, Lagos.
- Mr. A. Larval, Permanent Secretary, Federal Ministry of Health, Ikoyi, Lagos.
- Dr. Gaby Williams, Director, Public Health Services, Federal Ministry of Health, Ikoyi, Lagos.
- Dr. Brew - Graves, WHO Representative in Nigeria, Federal Secretariat, Ikoyi, Lagos.
- Dr. A.B. Suleman, Director of National Health Planning, Federal Ministry of Health, Ikoyi, Lagos.

3 - Contacts and technical discussions have been hold with the following professionals of Federal Vaccine Production Laboratory (FVPL), Yaba, Lagos:

- Dr. A. Nasidi, Consultant Virologist, Head of FVPL.
- Dr. G. M. R. Munube, WHO Virologist Consultant.
- Mr. A. O. Rufus, Chief Medical Laboratory Technologist.
- Dr. C. B. Coker, Head, of Quality Control Unit.
- Mr. O. Odutoyo, Head, of Administration Office.
- Mr. J. J. Ozogula, Head, Experimental Animal Unit.
- Mrs. M. E. Edozien, Head, Yellow Fever Vaccine Production.
- Mr. S. S. Oluyode, Head, Rabies Vaccine Production Laboratory
- Mr. S. A. Musa, Head, Maintenance Unit.
- Miss Owokoniran, D. Head, B.C.G. Vaccine.
- Mr. S. A. Egbewunmi, Diagnosis of AIDS.

A schematic chart of structure of FVPL is attached (annex 1).

4 - To enable the accomplisliment of technical consultancy, Dr. A. Nasidi, the head of FVPL has introduced me to the staff members and has asked them to provide me with information requested to enable a proper evaluation of YF vaccine production and control. Several meetings with specific groups and the visiting to the laboratories were them made.

There are two main FVPL laboratory compounds. The Central compound obrigates the direction of FVPL and laboratories of Quality Control, comprising the laboratory of experimental animal for YF vaccine potency determination, sterility and chemistry control. There are several other laboratories for diagnosis and surveillance of YF, Hepatitis, Measles and AIDS, and the laboratory for anti-rabies vaccine production.

The laboratory of Quality Control, besides doing the final control of YF vaccine produced at FVPL, analyses imported YF vaccines and the vaccines used in EPI vaccination.

The laboratory facility of Quality Control, at the time of visit, was undergoing changes and re-organization. To The laboratories, is being provivided better accomodations.

The basic equipments required for control were positioned at place and apparently are functioning.

Some of the last lots of YF vaccine titrated in this section is attached as annex 2; none of YF final product tested for bacterial sterility was positive.

It was possible to see the results of testing in the protocols positioned in each laboratories.

Very recently, during YF mass vaccination compaign a sero-conversion study was performed by Center of Disease Control/CDC, using YF vaccine produced at FVPL, Yaba and showed highly satisfactory results (annex 3).

The virology groups are preparing themselves to go into tissue culture technologies and may be able to titrate Yellow Fever Vaccine in tissue culture in near future.

5 - The Yellow Fever Vaccine is produced in the second compound which is about 1,5 km apart from central compound, is formed by several buildings:

Laboratory for Yellow Fevr Vaccine production, mice breeding, Rhesus monkeys colony, B.C.G. laboratory and maintenance workshop.

The Yellow Fever Laboratory/YFL was constructed in 1948 and originally was planned for a Hospital. It was adapted for YFV production and started this activity in 1952. The YFL comprisis 280 m^2 of area.

Although is newly painted, the facility is old and requires several improvements and critical modernization.

The YFL is organized comprising the following areas:

a) washing, preparation and sterilization, distilation of water;

b) steril area, provided with barrier (air-lock system) and an area for sterile cloth changing. The operations of eggs inoculation, embryo havesting, embryo homogenizing and macerating, collection of pulp, centrifugation, collection of embryo juice and filling are processed in this room. This area in well painted and very clean;

c) freeze-dryer room, next to sterile area;

d) freezer room;

e) experimental animal room;

f) chemistry room: for media preparation and sterility control. The incubation for eggs is placed in this laboratory. Next to this room, in a small room the virus dilution for mice titration is made;

g) Head Office;

h) Apart from main building are: laundry house, generator, incinerator, store house and maintenance workshop.

i) Office for senior staff and room for Junior staff.

The basic equipment required for production are positioned and are functioning, although most of them are very old and replacement parts are not available. To the most of equipments which requires temperature, vaccum or pressure recording, the register are attached but out of order. A list of existing equipment and its functioning status, prepared by the maintenance team is attached as annex 4.

6 - Procedures of YF Vaccine production 500 fertile eggs, brown, shell, supplied by a private local poultry firm are inocubated weekly. There are about 15% of loss among crushed and infertile eggs.

The seed-virus was received from Wellcome Laboratories in 1961 (annex 5). The inoculation is made on the amniotic membrane in 8 days old chickem embryo. After 4 days of incubation the harvest of embryo is performed. 25 embryo is collected in each blender-jar and 75 ml of phosphate buffer is added and homogenized. Thereafter, the pulp is collected, sheelfreezed and stored at -70 C. At this stage a sample is collected for sterility control and potency test. A very few contamination is observed, as it was registered in the protocol book. In the annex 6, 7 and 8 some further informations of their production are showed.

When the sterile control and potency testing are ready, enough quantities of pulps are thawed, centrifugated and embryo juice collected and pooled. A sample is again taken for sterility and potency testing. The pooled juice is splited in vials for freeze-drying, which is processed in a 48 hours cycle.

The vaccine is produced in 10, 20 and 40 doses presentation. A table with results of last 10 batches is attached as annex 6.

The current schedule for YFV production is established as follows:

a) at Wensdays: eggs incubation;

b) at Thursdays: eggs innoculation;

c) at Mondays: embryo harvesting;

d) at Tuesdays: liophylization.

This work-schedule is being operational. As result the vaccine production has augmented a very much (annex 7) in the current year.

The head of Laboratory Ms. M. E. Edozian has 15 years of experience in YFV production. She is graduated in biology sciences and is specialized in bacteriology. The Assistant to head Mr. J. J. Ozogula, principal technologist, has been working 16 years in vaccine production and 10 years in YFV production. Other members of technical staff seens to have also good laboratory skills but if they receive some more support such as specific training courses, should be able to colaborate and participate intensively in the modernization and upgrading project.

The leaflet of YF vaccine, Yaba, Lagos is attached as annex 8.

7 - Although the YFV laboratory is operating routinelly, several important constraints exists, as follows:

- the washing and sterilizing capacity is very small;
- the sterile area is very small;
- the flow of production presents several crossing points;
- the freeze-dryers are of small capacity;
- the maintenance staff members are not specialized and are not part of production team;
- the short-curt of power occurs almost every day, even though they have back up generators;
- the supplies, glassware and spare parts are not enough;
- financial constraints, particulary the runing cost budgest is very low.

8 - After several meetings and discussions with FVPL staff members, with active participation of the Head of FVPL, Dr. A. Nasidi and WHO virologist consultant, Dr. S. M. R. Munube the following documents were prepareand are attached as annex 9:

a) the outline of the project for modernization and upgrading YFV production, Yaba;

b) preliminary drawing for the modernization and upgrading YFV production laboratory;

c) alternative lay-out for right wing.

d) preliminary drawing for diluent production.

e) current lay-out of YFV production laboratory.

The FVPL will fill the IDRC application form using the outline of the project attached, and will send it to IDRC/Regional Office for Africa in Senegal/Dakar, as soon as they receive the application form.

To make possible further steps towards the modernization a private especialized firm was contacted and arragments is being made for the preparation of engineering project. According to the Ministry of Health authorities this is a priority project and a special budgest will be alocated to make possible the execution of YF laboratory modernization.

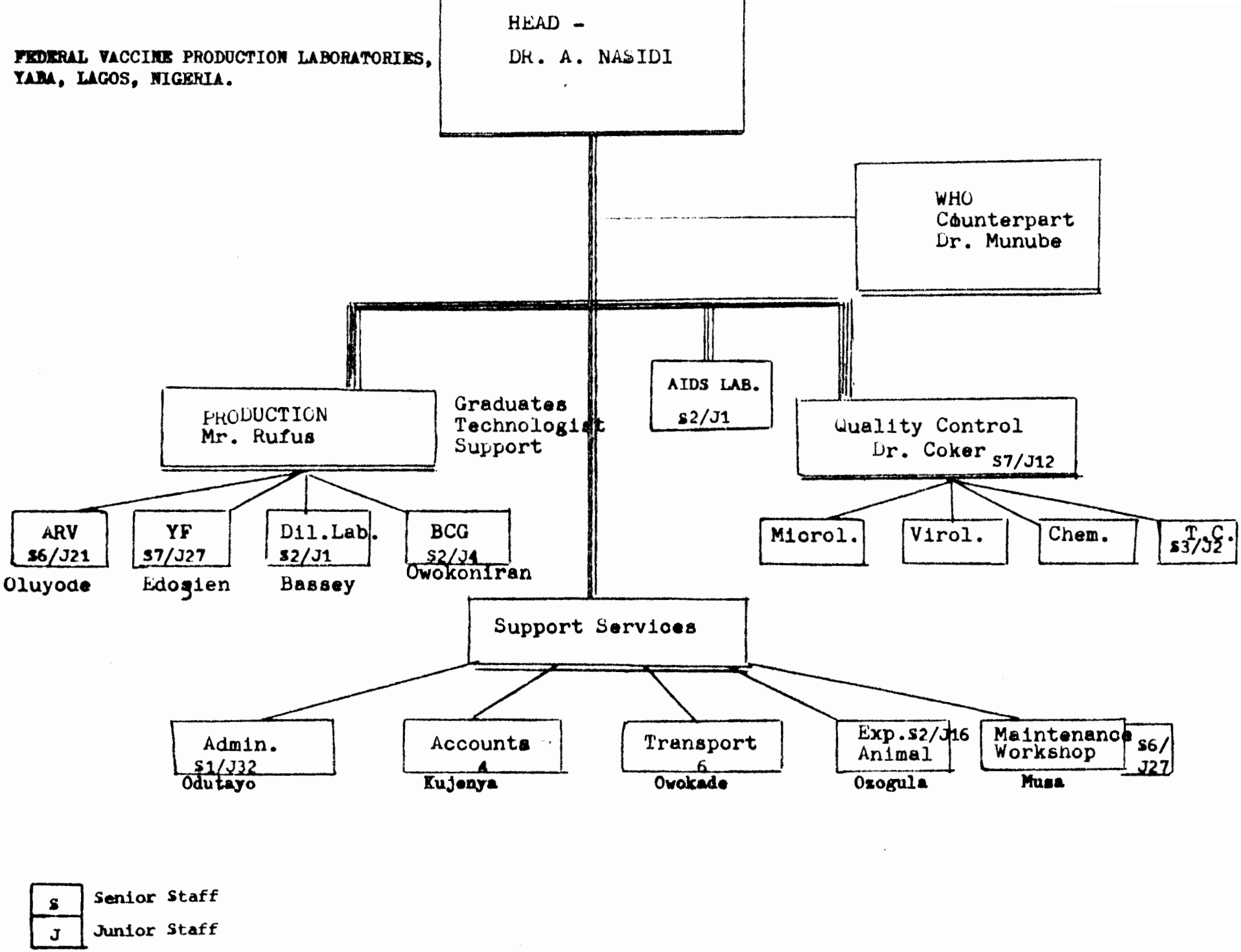
9 - As Nigeriam Ministry of Health is planning a new complete center for vaccine production needed for EPI in Abuja, the new capital of Nigeria, this project could be very important, as additional motivating factor by functioning as demonstration project of Nigeriam biological technology capabilities.

10 - These documents were also presented to the Minister of Health Professor Ransome-Kuti, to the Permanent Secretary Mr. A. Lawal and to Dr. Gaby Williams, Director of Public Health Services. A strong committment from all above authonites of Ministry of Health was obtained to support this project.

Ibn, October 22nd 1987

DR. AKIRA HOMMA

FEDERAL VACCINE PRODUCTION LABORATORIES, YABA, LAGOS, NIGERIA.



ANNEX 2

7th October, 1987.

SOME YELLOW FEVER VACCINES RECEIVED AND TESTED BY THE QUALITY CONTROL UNIT, FEDERAL VACCINE PRODUCTION LABORATORIES

	LOT NO.	ORIGIN	DATE TESTED	BY ANIMAL INOCULATION TITRE LD50	LOG 10	RESULT
1	YFV . 593	FVPL Lagos Nigeria	28/1/87	LD50=937/0.5ml (human dose)	2.97	Rejected
2.	YFV . 594	FVPL	28/1/87	LD50=3568/0.5ml (human dose)	3.55	Good
3.	YFV . 595	FVPL	24/2/87	LD50=1442/0.5ml (human dose)	3.16	Good
4.	YFV . 596	FVPL	6/4/87	LD50=1037/0.5ml (human dose)	3.02	Good
5.	YFV . 597	FVPL	24/6/87	LD50=3732/per (human dose)	3.57	Good
6.	YFV . 599	FVPL	25/6/87	LD50=1004/0.5ml	3.00	Good
7.	YFV . 601	FVPL	25/6/87	LD50=2899/0.5ml (human dose)	3.46	Good
8.	YFV . 603	FVPL	25/6/87	LD50=4807/0.5ml (human dose)	3.68	Good
9.	YFV . 605	FVPL	25/6/87	LD50=2645/0.5ml (human dose	3.42	Good
10.	YFV . 607	FVPL	19/8/87	Ld50=1913/0.5ml (human dose)	3.28	Good
11.	YFV . 609	FVPL	20/8/87	LD50=3818/0.5ml (human dose)	3.58	Good
12.	YFV . 611	FVPL	20/8/87	LD50=1667/0.5ml (human dose)	3.22	Good

S. O. Johnson
Scientifie Officer . I.

cc: DR. A. Y. Kasidi-Consultant Virologist.

" DR. C. B. Coker-Principal Virologist.

" DR. Munube - WHO Consultant Virologist.

ANNEX 3

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Centers for Disease Control

Center for Infectious Diseases
Division of Vector-Borne Viral Diseases
P. O. Box 2087
Fort Collins, CO 80522-2087
(303) 221-6428

January 23, 1987

Dr. A. Nasidi
Consultant Virologist
Federal Ministry of Health
Vaccine Production Laboratory
PMB 2010
Yaba, Lagos
Nigeria

Dear Dr. Nasidi:

We have completed neutralization tests on the children bled on 19 December, 1986. These children had been vaccinated on 31 October, 1986, with Yaba vaccine (expiration date, October 1986). Fifty-three sera were obtained; two sera were missing (blood may not have been obtained from these children). Of the 51 sera tested, 50 (98%) had detectable yellow fever neutralizing antibodies. Four children had low titers (1:2) or insufficient serum was available to test at higher dilutions.

The seroconversion rate in this population is excellent and consistent with previous studies which generally show 95% or greater rates after administration of 17D vaccine.

The seronegative child (No. 263, Lydia Otiyunge) should be re-immunized. It would not be unreasonable to re-immunize the 4 children with titers of 1:2, although they are probably protected.

Warmest personal regards,

Sincerely yours,

Tom

Thomas P. Monath, M.D.
Division Director

TPM:dgl

cc: Dr. Kevin DeCock (With Table)
Dr. Bruce Cropp (With Table)

EQUIPMENT INVENTORY IN YELLOW FEVER VACCINE LABORATORY

LIST OF EXISTING EQUIPMENT		MODEL OR SERIAL NO	YEAR OF ACQUISITION	STATE OF OPERATION	EXISTING SPARE PARTS
DEEPFREEZERS (ULTRA-LOW)	2 NO	PUFER HURBAR	1986	SATISFACTORY	NIL
" "	2 NO	REVCO	1950"	BAD	NIL BUT CAN BE REACTIVATOR
"	3 NO	FROSTCOLD	1960"	SATISFACTORY	NIL
"	3 NO	LEC	1970"	"	NIL
"	1 NO	SANYO	1970"	"	NIL
FREEZE DRYERS	2 NO	EDWARDS EF.6	1972	one not satisfactory	LIMITED SPARES
" "	1 NO	" LYOKAST 508	1984	Satisfactory	ALL NECESSARY SPARES TO LAST TWO WORKING YEARS EXCEPT COMPLETE CONDENSING UNIT WAS NOT INCLUDED IN THE SUPPLY.
EGG INCUBATORS (BIG SIZE)		MAYFAIR	1982	"	NIL
SMALL "		SIZE 1	1982	"	NIL
" "		" 2	1984	"	1, FAN MOTOR; 2 CASTOR ROLLER AND FUSES
WOODEN TYPE "		CHARLES HEARSON	1950"	BAD	BEYOND ECONOMIC REPAIRS
AUTOCLAVES	3 NO	BAIRD & TATLOCK	1960"	SATISFACTORY	I SET HEATING ELEMENT ONLY
" STEAMS		GRIFFINS GEORGE	1960"	"	NIL
SHELL FREEZING		VIRTIS	1950"	ERRACTIC	NIL
HOT AIR OVEN	2 NO	LTE	1950"	FAILY GOOD	NIL
" " "	2 NO	ETL	1960"	"	NIL
CENTRIFUGES (TABLE MODEL)	2 NO	MSE	1960"	SATISFACTORY	NIL
REFRIGERATED CENTRIFUGE	1 NO	MSE	1960"	FAIRLY	NIL
GENERATING PLANT 14.6KVA		LISTER	1985	SATISFACTORY	NIL
" " 12KVA		"	1975	"	NIL
WATER BATH	2 NO	MEMMERT	1960"	"	NIL
" "	1 NO	GRIFFINS GRINDY	1950"	BAD	CONTROL BOX MISSING
" "	1 NO	BAIRD & TATLOCK	1950"	ERRACTIC	NIL

NOTE: WE HAVE JUST INITIATED THE POLICY OF REQUESTING SUPPLIERS TO SUPPLY TWO YEARS RUNNING SPARES WITH EQUIPMENT HENCE ITEMS 7 & 10 ABOVE OTHERWISE THERE HAD NEVER BEEN ANY WITHOLDING SPARES.

ANNEX 5

Yellow Fever Vaccine Lab.,
Yaba,
Lagos.

13th October, 1987.

The Consultant Virologist,
Vaccine Production Laboratory,
Yaba.

SEED VIRUS ORIGIN

The Seed Virus registered in Yaba as PS_3, was received from Burroughs Wellcome Laboratories, Beckenham, Kent England in November 1961. This seed virus is the 6th egg passage of 225th subculture of the 17D Yellow Fever Virus.

The Secondary seed virus designated as S_2PS_3 was prepared from PS_3 in July, 1972 and a fresh batch of S_2PS_3 was prepared by the Unit in July, 1986.

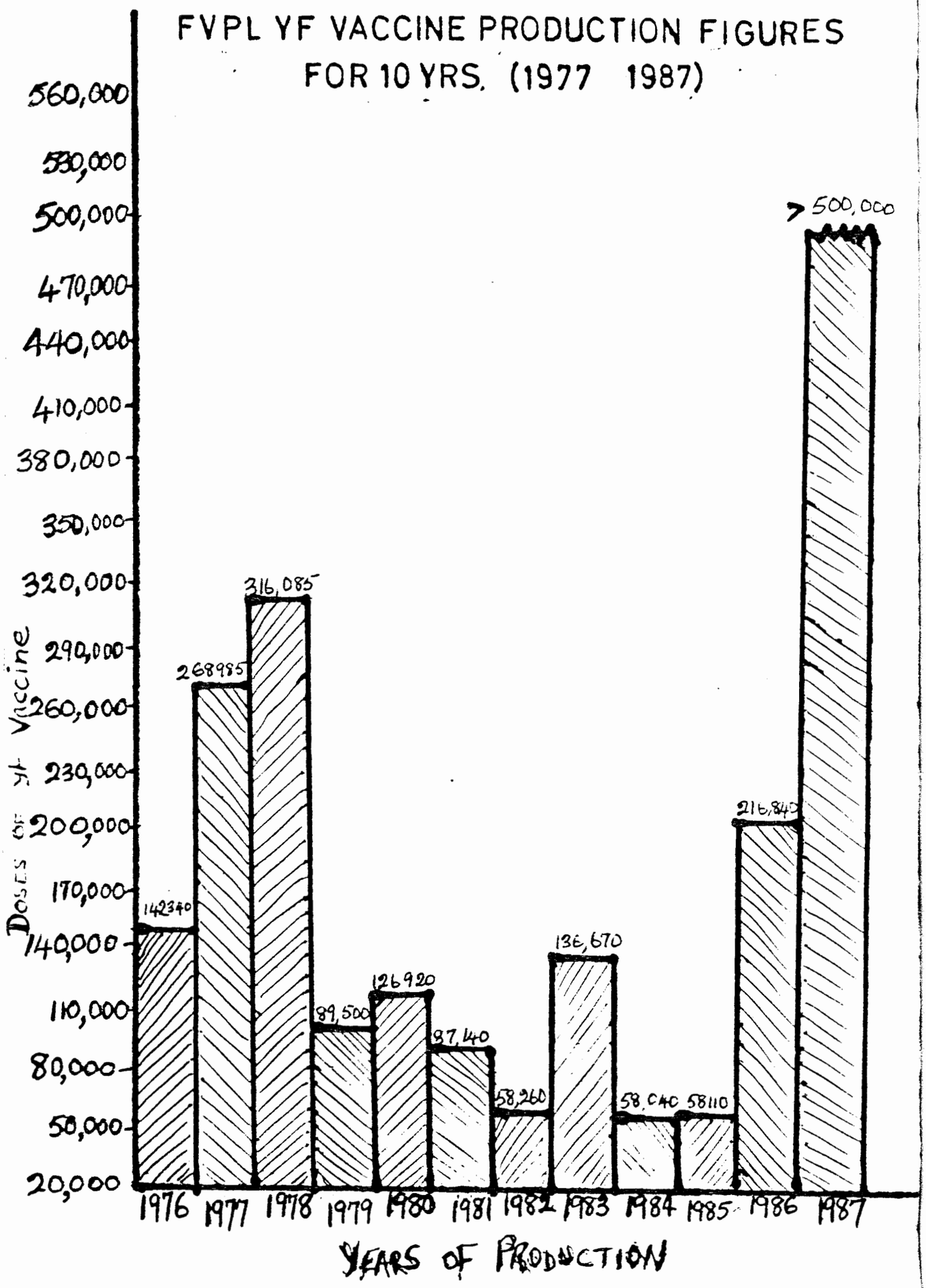
Thank you.

M. E. EDOZIEN
Principal Med. Lab. Technologist.

BATCH NO	SEED VIRUS TYPE	PULP TITRE	EMBRYO JUICE TITRE	FREEZE DRY TITRE	
590	$10^{-1.9}$/0.03ml 333, $LD/_{50}$ per egg/0.125ml	$10^{-4,0}$ 333,333 $LD/_{50}$ per ml (5.52ml)	$10^{-3.07}$ 39,000 $LD/_{50}$ per ml (46ml)	$10^{-2.46}$ 4,874 $LD/_{50}$ per dose (40) ml	
591	$10^{-2.88}$ 851 $LD/_{50}$ per egg/0.125ml	$10^{-4.0}$ 333,336 $LD/_{50}$ per ml (5.52ml)	$10^{-3.92}$ = 277,266 $LD/_{50}$ per ml (5.44) ml	$10^{-3.40}$ 41,856 $LD/_{50}$ per dose (492ml)	
592	$10^{-2.6}$ = 1658 $LD/_{50}$ per egg/0.125ml	$10^{-4.5}$ 1,054,000 $LD/_{50}$ per ml (6.02ml)	$10^{-4.16}$ =481,666 $LD/_{50}$ per ml (5.68ml)	$10^{-3.47}$ 52,700 $LD/_{50}$ per dose 5.02ml)	
593	$10^{-2.75}$ = 2343 $LD/_{50}$ - per egg/0.125ml	10^{-4-32} 696,333/$LD/_{50}$ per ml (5.84) ml	$10^{-4.24}$ 577,33 $LD/_{50}$ per ml (5,76ml)	$10^{-3.47}$ 49,183 $LD/_{50}$ per dose (4.99ml)	
594	$10^{-10-2.75}$ 2343 $LD/_{50}$ per egg/0.125ml	$10^{-5.0}$ 3.3 x 10^{6} $LD/_{50}$ per ml (6.5ml)	$10^{-4.18}$ = 500,666 $LD/_{50}$ per ml (5,70ml)	$10^{-3.31}$ 34,029 $LD/_{50}$ per dose (4.5ml)	

BATCH NO	SEED VIRUS TYPE	PULP TITRE	EMBRYO JUICE TITRE	FREEZE DRY TITRE	
595	$10^{-2.5}$ = 2065 LD/50 per egg/0.125ml	$10^{-4.5}$ =1,050,000 $LD/_{56}$ per ml (6.02ml)	$10^{-4.16}$ 481,666 $LD/_{50}$ per ml (5.68ml)	$10^{-3.12}$ 21,966 $LD/_{50}$ per ml dose (4.64ml)	
596	$10^{-2.88}$ = 3160 $LD/_{56}$ per egg/0.125ml	$10^{-4.6}$ 1,327,000 $LD/_{56}$ per ml (6.12ml)	$10^{-4.00}$ 333,333 $LD/_{50}$ per ml (5.52ml)	$10^{-3.00}$ 16,600 $LD/_{50}$ per dose (4.52ml)	
597	$10^{-2.6}$ = 1658 $LD/_{50}$ per egg/0.125ml	$10^{-4.5}$ 1,05.4000 $LD/_{50}$ per ml (6.02ml)	$10^{-4.25}$ = 592,666 $LD/_{50}$ per ml (577ml	$10^{-3.16}$ =24,800 $LD/_{50}$ per dose (4,70)	
598	$10^{-2.63}$ 1778/ $LD/_{50}$ per egg/0.125ml	$10^{-4.5}$ 1,054.00 $LD/_{50}$ per ml (6.02/ml	$10^{-4.17}$ =493,000 $LD/_{50}$ per ml (5.69/ml	$10^{-3.0}$ =16,600 $LD/_{50}$ per dose (4.52/ml	
599	$10^{-2.5}$ = 1318 $LD/_{50}$ per egg/0.125ml	$10^{-4.13}$ 450,000 $LD/_{50}$ per ml (5.65/ml)	$10^{-3.0}$ 33,333 $LD/_{50}$ per ml (4.52/ml	$10^{-2.67}$ = 7,795 $LD/_{50}$ per dose (4.19/ml	

ANNEX 7


FVPL YF VACCINE PRODUCTION FIGURES
FOR 10 YRS. (1977 1987)
560,000
530,000
500,000
470,000
440,000
410,000
380,000
350,000
320,000
290,000
260,000
230,000
200,000
170,000
140,000
110,000
80,000
50,000
20,000
Doses of YF Vaccine
142340
268985
316,085
89,500
126920
87,140
58,260
136,670
58,040
58110
216,845
> 500,000
1976
1977
1978
1979
1980
1981
1982
1983
1984
1985
1986
1987
YEARS OF PRODUCTION

ANNEX 8

FREEZE-DRIED 17D YELLOW FEVER VACCINE FOR SUBCUTANEOUS USE

1. GENERAL INFORMATION

This vaccine is a live, attenuated freeze-dried (lyophilized) product prepared from an extract of chick embryos inoculated with 17D strain of yellow fever virus. The vials are sealed in the atmosphere of dry nitrogen gas. The vaccine is sensitive to heat and light and must, therefore, be stored according to instructions. It is used for protection against yellow fever.

2. INDICATIONS

- For protection against yellow fever in endemic areas or during yellow fever epidemics
- As a requirement for internation travel.

3. CONTRA-INDICATIONS

Sensitivity to egg proteins, generalized malignancies, immuno-supressive states whether in-born or acquired, severe febrile illness, pregnancy, infants under 12 months of age except in the face of an epidemic when infants 6 months and over may be vaccinated.

4. PRECAUTIONS/WARNINGS

A 1:1000 epinephrine (adrenaline) should be available when giving vaccines in case anaphylactic reaction develops.

5. ADVERSE REACTIONS

Except for anaphylactic reaction in individuals sensitive to egg protein or those with above-mentioned contra-indications, adverse reactions to 17D yellow fever vaccine are extremely rare.

6. DOSAGE AND ADMINISTRATION

(a) **Warning**

Aseptic measures must be taken in any of the steps leading to the administration of the vaccine. The vials must be examined carefully and broken or cracked ones should be discarded. Expired vaccine should not be used.

(b) **Reconstitution**

For reconstitution of the vaccine, use the recommended, chilled diluent in volumes consonant with the doses in the vials (2.5ml for 5 doses, 5 5ml for 10 doses, 11ml for 20 doses, 27ml for 50 doses).

Keep the reconstituted vaccine on wet ice or in a refrigerator at (+2–8=C) until all doses have been used. In any case, the reconstituted vaccine should be used within one hour. Any volume of the vaccine that remains after each vaccination session should be discarded on the same day.

(c) Dosage

The human dose for both children and adults of the reconstituted vaccine is 0.5ml given subcutaneousiy over the deltoid area of the arm.

ANEX 9-a

Project Title: Modernization and Expansion of the Yellow Fever Vaccine Laboratory, Federal Vaccine Production Laboratory, Yaba, Lagos, Nigeria.

Project Leader: Dr. A. Nasidi,
Federal Vaccine Production Laboratories,
Yaba, Lagos.

SUMMARY

Yellow fever, an acute viral disease, is still a troublesome public health problem in the tropical area of Africa. Periodically recurring epidemics cause thousands of cases and deaths as evidenced by the recent outbreaks of the disease in Nigeria. Besides, vaccination to control yellow fever epidemics, the Federal Ministry of Health has strongly committed itself to the inclusion of yellow fever vaccination in the Expanded Programme on Immunization as a measure of increasing herd immunity of the population in the coming years. The demand of the yellow fever vaccine will consequently markedly increase. The Federal Vaccine Production Laboratory, Yaba, Lagos is embarking on measures towards modernization, upgrading and strengthening the capabilities of production and quality control so that the vaccine produced will satisfy all the WHO minimum requirements especially those related to thermostability.

The modernization and upgrading project includes improvement of the physical facilities, provision of new equipment and supplies and the training of staff. The excution of the project will require external assistance to supplement the effort of the Federal Ministry of Health of the Federal Republic of Nigeria.

When the project is fully implemented, Nigeria will be self-sufficient in high quality, thermostable yellow fever vaccine and could even be in a position to supply vaccine to other needy countries in the region.

The reorganization of the present Federal Vaccine Production Laboratory, Yaba will require a serious investment, as detailed in the proposal.

BACKGROUND

1. Yellow Fever is an acute infectious disease caused by a virus transmitted to humans by mosquitoes. The virus is maintained in nature by monkey-mosquito - monkey cycle. The main clinical features include fever, jaundice and haemorhagic manifestation. During epidemics, the case fatality rate has been observed to range from 20-80%. Deaths are usually associated with renal, hepatic or cardio-vascular failures. In the absence of an effective treatment, the only available method of management is the administration of symptomatic treatments.

2. In Africa, outbreaks or epidemics of Yellow Fever (YF) occur periodically in endemic areas, stretching from latitude 15°N to 10°S. Countries lying between these latitutes have experienced more than one epidemic of YF over the last 50 years, each epidemic being associated with high death rate. For example, in 1960-62 a very serious epidemic involving 100,000 people with an estimated 30,000 deaths, was experienced in Ethiopia. In West African Countries, similar serious epidemics have occurred in countries like Senegal(1965-20,000 cases/6,000 deaths), Nigeria(1969-10,000 cases/ 4,000 deaths), Gambia(1978-79 - 8.400 cases-1,600 deaths), Burkina Fasso (1983-25,000 cases-1,400 deaths) and again in Nigeria(1986-87 estimation 50,000 cases with 12,000 deaths). Obviously, there are minor outbreaks in between these big epidemics which occur without attracting the attention of the Public Health Authorities. The figures presented above do not, most probably represent the true picture of cases and deaths that do occur during these epidemics, but are however sufficient to depict the gravity of the YF situation in Africa.

3. In most of the YF epidemics recorded in Africa, the following species of Aedes mosquitoes have been incriminated in the transmission of the disease; namely Aedes africanus, Ae. lutheocephalus, Ae. fulcifer/taylori, Ae. Simpsom, Ae. aegypti, etc. In addition, Ae. aegypti, the urban vector of YF can be found in many villages and towns. During the recent YF epidemic in Nigeria (1986-87) in Oju, Benue State and Ogoja, Cross River State, the main mosquito vector was found to be Ae. africanus. However, in the Oyo epidemic(April-October,1987). Ae. aegypti was the only vector involved.

4. The main approach for the prophylaxis of yellow fever, besides the vector control in the urban area, is the vaccination of susceptible population. There is an excellent vaccine against yellow fever, which seed virus strain and technology was developed in the early thirties by the Rockefeller Foundation. Basically, it consists of infecting growing chick embryo with attenuated virus(17D strain) and recovering of vaccine virus from embryo tissues. The vaccine must be freeze-dryed because of its easy and rapid thermo degradation.

   In the last few years the technology of Yellow Fever Vaccine Production has been very much improved. It involves the use of a well defined chick embryo(like SPF eggs),the thermo stabilization of vaccine, adoption of Good Manufacturing Practices(GMP) and Minimal Requirements documented in the Technical Report Series and other related publications of the World Health Organization, which include high standards of laboratory facilities for both production and quality control.

..../2

5. It is known that the Yellow Fever Vaccine is one of the safest and most effective vaccines available. A single potent dose of this vaccine is enough to provide protection to the vaccinee for at least 10 years, if not for life. Despite the availability of such a safe and effective vaccine against this disease, the epidemics continue to be experienced in a number of African countries, including Nigeria. This is largely due to the absence of well-defined, prophylactic vaccination programmes or policies. Mass vaccinations are only carried out in response to epidemics. Such approaches, apart from being expensive in terms of human, material and financial resources, do not provide long term solution to the problem.

The absence of a national policy on regular vaccination against YF in Nigeria has contributed to the under development of the available facilities for the production of Yellow Fever Vaccine(YFV) in the Federal Vaccine Production Laboratory(FVPL) Yaba, Lagos.

6. The Federal Vaccine Production Laboratory(FVPL) was created from the Rockefeller Yellow Fever Laboratory, which was established in 1925. In the early 1930s the Laboratory started producing smallpox vaccine in sheep. This Laboratory contributed enormously towards the total eradication of smallpox in West Africa. The production of Anti-rabies vaccine(ARV) was started in 1948, and the vaccine was produced in sheep brain using the Semple methodology. Presently, the Laboratory produces an average of 25,000 doses of ARV for human use annually. The method of production ensures complete inactivation of virus using phenol.

In 1952, the production of YF was started; and by 1956, the locally produced vaccine was approved by the WHO. Presently the annual production capacity is about 1,200.000 doses. The actual annual average production level for the last 10 years has been about 120,000 doses per year. Such low level of production is caused by several constraints. However, production of 500,000 doses is being attained this year just by the introduction of an effective managerial system.

7. In addition, the FVPL provides important laboratory support for crucial public health programmes such as the surveillance and diagnosis of viral diseases(YF, hepatitis, measles and AIDS) and the monitoring of the potency and efficacy of Expanded Programme on Immunization(EPI) vaccines.

The World Health Organization has been actively associated with the activities of the(FVPL) for several years through the provision of technical and professional personnel and certain equipments and materials. This collaboration is continuing and presently a WHO Consultant Virologist is attached to the FVPL.

8. The present FVPL administration has been able to obtain increased encouragement and support from the Federal Minister of Health to the effect that concrete measures have been initiated towards the up-grading and expansion of the Yellow Fever Vaccine Laboratory(YFVPL). For example, money was made available for the regular supply of fertile eggs on annual basis as against the former supply system, based on ad hoc arrangements. Money was also made available for the procurement of a large quantity of vials, rubber stoppers and aluminium caps, required to cover a long period of production. These developments have enabled the achievement of increased level of production by about 5 times. This shows that there is a capable Technical staff at the Federal Vaccine Production Laboratory which could be put to greater use, if the facilities were fully supported, modernised and up-graded.

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The reorganization of personnel and creation of some additional units in the Quality Control Section, has contributed to the attainment of better performance.

9. Because of the recent large epidemics of YF in the country, the authorities of the Federal Ministry of Health are strongly committed to include the vaccination against Yellow Fever in the EPI which today includes OPV, Measles and DPT vaccination. This has been approved by the Federal Minister of Health and adopted as a policy. Several experts, including those from the World Health Organization, who studied the recent Nigerian Yellow Fever outbreak produced some important documents, in which the inclusion of YFV in the EPI was also strongly recommended.

The inclusion of YFV in the EPI will necessitate an annual requirement of 5 to 6 million doses of YF vaccine (Nigeria's annual birth rate:4.5 million infants).

10. To ensure the supply of such large quantities of YFV on a continuous basis, it is imperative that the country produces this vaccine in sufficient quantity to meet at least its domestic requirements. This is so, because of the fact that such a large quantities of the vaccine will increase appreciably the cost of EPI.

The experts from WHO have strongly recommended the modernization of strengthening of the YFV and production facilities at Yaba. This will involve the manufacture of thermostable vaccine and the adoption of the recommended quality control requirements.

11. The Federal Ministry of Health has also made a strong commitment to make investments required to modernize and to strengthen the YFV facilities. But, the external collaboration in all steps of this three-year project is of uttermost importance, especially those related to the supporting of the training of local personnel abroad in a Yellow Fever Vaccine Producing Institution, providing new laboratory equipment, imported supplies and some stationery resources.

OBJECTIVES

12. The objectives of this project are:

(a) to promote the modernization and the strengthening of Yellow Fever Vaccine Laboratory facilities at Yaba, Lagos.

(b) to promote the adoption, in all steps of production and quality control of Good Manufacturing Practices and to ensure their compliance with WHO Requirements.

(c) to promote the up-grading of the vaccine production laboratory to manufacture increased quantities and improve the quality of the vaccine with introduction of thermostable formulation.

METHODOLOGY

13. Initially, a critical evaluation of the facility was performed. An analysis of the flow of production, which included the appraisal of the condition of equipments, the evaluation of quality control system, the production and quality control procedures was carried out.

14. To enable further actions for modernization to be taken, a preliminary drawing of the facility was prepared(attach. 1). It takes into account, whenever possible, the flow of production, avoiding cross movements combining compatible activities and protecting areas for sterile operations. In a separate building in the same compound, a drawing for a diluent production facility was also prepared(see attch.2).

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15. A summary of this study was also submitted to the authorities of Ministry of Health and a commitment to support this project was assured.

The cost of modernization has been estimated at US $4,000,000 and will be largely supported by the Federal Ministry of Health. Already, an amount of about US $1,500,000 is being set aside for this project by the Federal Ministry of Health.

16. To make possible the modernization of the facility at low cost, the proposal takes into account the existing walls of the present building with only minor additions to be made.

Bearing in mind the nature of the modernization envisaged, a new electrical wiring system, a centralized air-conditioning system, central steam generator, an over-head tank, replacement of existing water pipes and incoporation of hot water supply will be required. An additional high capacity generator with automatic switch system will also be required.

17. In view of the present unfavourable economic situation of Nigeria, the expenditure on imported equipment, materials and supplies will be very difficult. Therefore external assistance to help in the acquisition of these items is strongly needed. A list of the major equipment as well as other needed materials and supplies is needed in the budget table.

TRAINING

18. The YFVPL, Yaba employs 16 graduates/professionals and has an adequate number of supporting staff. During the modernization period the production activities will be reduced to the minimum. This period will be used for the training of selected technical and scientific staff abroad, preferably at Yellow Fever Vaccine producing laboratory or institution e.g. FIOCRUZ, Brazil.

It is recommended that 9 members of staff would be trained or retrained on a recycling basis in the areas of YF vaccine production(2), animal breeding and testing(4), Quality Control(2), Microbiology(1), Chemistry(1), Tissue Culture(4), Diluent production(1) and laboratory equipment maintenance(2). For these staff members, the period of training will vary from 1-3 months.

Additionally, the Director(Consultant Virologist) and the WHO Consultant Virologist attached to the project should make short visits to selected laboratories for the period of not less than 2 weeks.

CONSULTANCY

19. For the attainment of faster and effective results of the modernization and achievement of set goals, it is advisable to engage the services of consultants on various aspects, who will be visiting the facilities during the modernization and after upgrading. These consultants will be required in the areas of engineering/maintenance and in the latest production and quality control technologies. It will be preferable if the consultants on production technology and control could come from the institution where the FVPL staff will be trained.

ADMINISTRATION AND BUDGET

20. This 3-year project will be administered by the Federal Vaccine Production Laboratory of the Federal Ministry of Health. A special account will be opened in the name of the project in a bank, with the Permanent Secretary or his designated representative and the Head of the FVPL be co-signatories of the Cheques.

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It is estimated that the cost of equipment, materials will be CAN $585,600.00 and the supplies will be CAN $73,000.00.

The training programme and consultancy will cost CAN $130,500.00.

The money for the Stationery will be CAN $42,000.00.

The total project value will be CAN $789,100.00.

TO BE ADMINISTERED BY THE RECIPIENT	IDRC CONTRIBUTION (IN CAN DOLLARS) YEAR 1	YEAR 2	YEAR 3	TOTAL	NIGERIA MOH/FVPL(IN NAIRA ₦) YEAR 1	YEAR 2	YEAR 3	Total
1-Personnel								
1-Coordinator Consultant Virologist (24 person - months)	-	-	-		7,400	7,400	7,400	22,600
1-Principal Medical Lab. Technologist (36 person - months)	-	-	-		8,700	8,700	8,700	26,000
2-Senior Medical Lab. Technologist (36 person - months)	-	-	-		14,000	14,000	14,000	42,000
8-Medical Lab. Technologist (36 person - months)	-	-	-		46,080	46,080	46,080	138,240
5-Scientific Officer (36 person - month)	-	-	-		22,620	22,620	22,620	67,860
2-Principal Maintenance Officer (6 person - months)	-	-	-		17,364	17,364	17,364	52,092
12-Lab. Assistance (36 person - months)	-	-	-		20,880	20,880	20,880	62,640
10-Lab. Attendants (36 person - months)	-	-	-		15,960	15,960	15,960	47,880
Sub-total	-	-	-		153,004	153,004	153,004	459,012
2. Stationery	10,000	10,000	10,000	30,000	40,000	40,000	40,000	120,000
3. Communications	3,000	3,000	3,000	9,000	5,000	5,000	5,000	15,000
4. Final Reports	-	-	3,000	3,000	8,000	8,000	8,000	24,000
Total Recipient administered funds	13,000	13,000	16,000	42,000	206,004	206,004	206,004	618,012

IDRC CONTRIBUTION (CAN$)

TO BE ADMINISTERED BY IDRC	YEAR 1	YEAR 2	YEAR 3	TOTAL
1. EQUIPMENT:				
1 Freeze-dryer, plus acessories and spare parts	160,000	-	-	160,000
1 Filling and stopper machine, plus acessories and spare parts	120,000	-	-	120,000
1 Automatic vial wash machine, plus acessories	87,000	-	-	87,000
1 Refrigerated centrifuge, plus Rotor, acessories and spare parts	18,000	-	-	18,000
1 Reverse Osmose Water purification	35,000	-	-	35,000
3 Suspended Vertical Laminar flow unit, with accessories	38,000	-	-	38,000
2 Egg incubator complete with automatic revolving	18,000	-	-	18,000
2 Wath distilater	7,000	-	-	7,000
1 Shell freezing machine	2,000	-	-	2,000
3 Sterilising oven	12,000	-	-	12,000
1 Labelling machine (semi-automatic)	12,000	-	-	12,000
2 Egg candling machine	5,000	-	-	5,000
2 Autoclave horizontal	8,600	-	-	8,600
2 Deep Freezer - 85°C with accessories and spare parts	20,000	-	-	20,000
Experimental animal cages (for guinea pigs, rabbits, mice) plus shelves, bottles and accessories	16,000	-	-	16,000
10 Mobile racks for cage	16,000	-	-	16,000
2 Filter Holder with acessories	10,000	-	-	10,000
Sub Total	585,600	-	-	585,600
2. SUPPLIES				
- Spare parts for existing equipments	10,000	10,000	10,000	30,000
- Glassware	10,000	10,000	10,000	30,000
- Reagents and media	2,000	2,000	2,000	6,000
- Shipping	5,000	1,000	1,000	7,000
Sub-total	27,000	23,000	23,000	73,000

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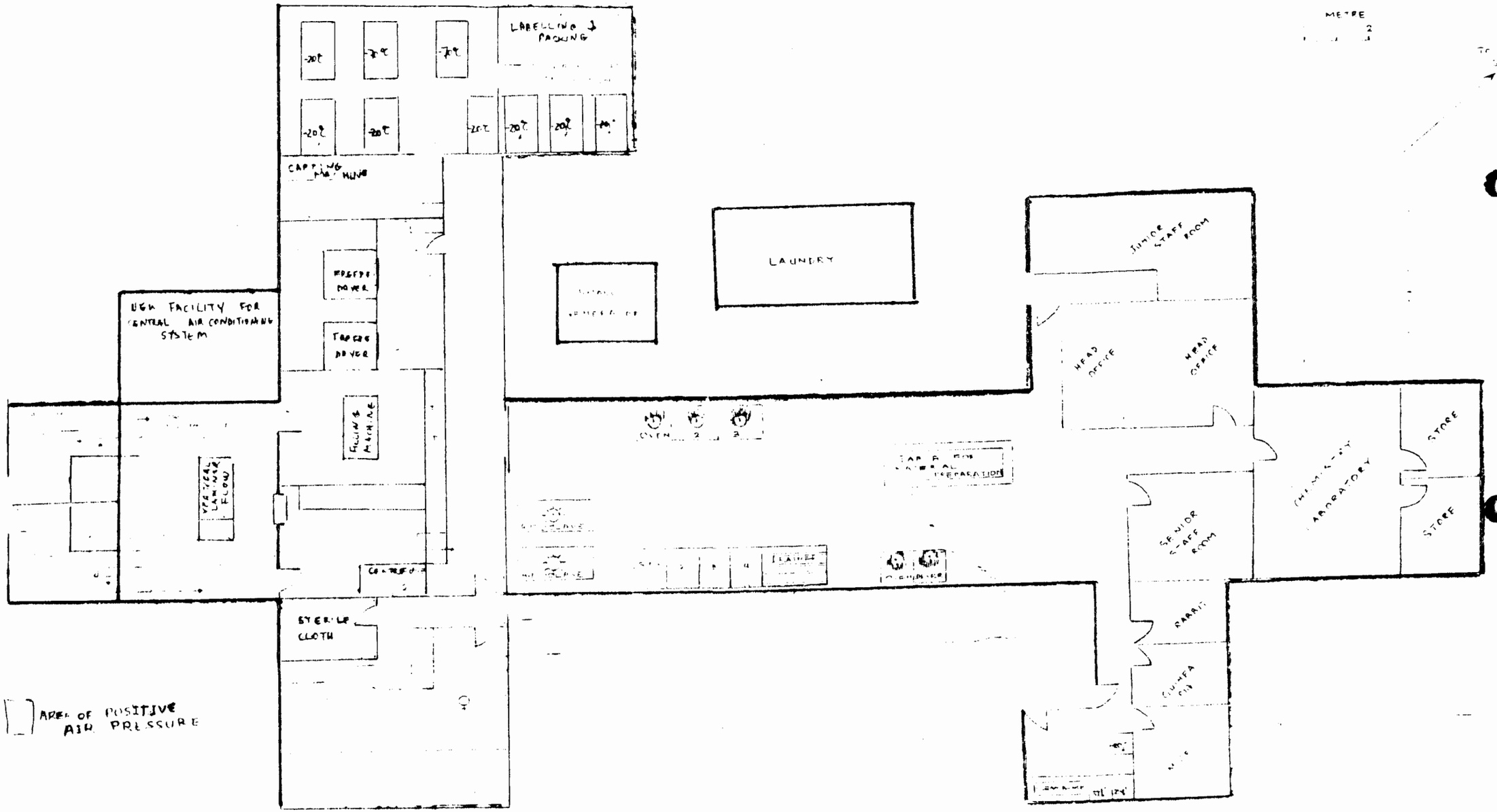
IDRC CONTRIBUTION (CAN$) CONTD.

TO BE ADMINISTERED BY IDRC	YEAR 1	YEAR 2	YEAR 3	TOTAL
3. TRAINING				
2-Cordinator + WHO Consultant	9,000	-	-	9,000
2-Principal Medical Lab. Technologist	9,000	-	-	9,000
6-Senior Medical Lab. Technologist	18,000	18,000	18,000	54,000
2-Maintenance	-	18,000	-	18,000
Sub-total	36,000	36,000	18,000	90,000
4. CONSULTANT VISITING				
1-Project development	4,500	4,500	4,500	13,500
1-Equipment maintenance	-	4,500	4,500	9,000
1-Production operation	-	4,500	4,500	9,000
1-Quality Control	-	4,500	4,500	9,000
Sub-total	4,500	18,000	18,000	40,500
TOTAL.....	653,100	77,000	59,000	789,100

Total IDRC administered portion CAN$	789,100.00
Total FVPL administered portion CAN$ (Stationery, communication, final Report)	42,000.00
Total of the project in Candian dollars CAN$	831,100.00

Annex 9-b

YELLOW FEVER VACCINE LAB: (PROPOSED)



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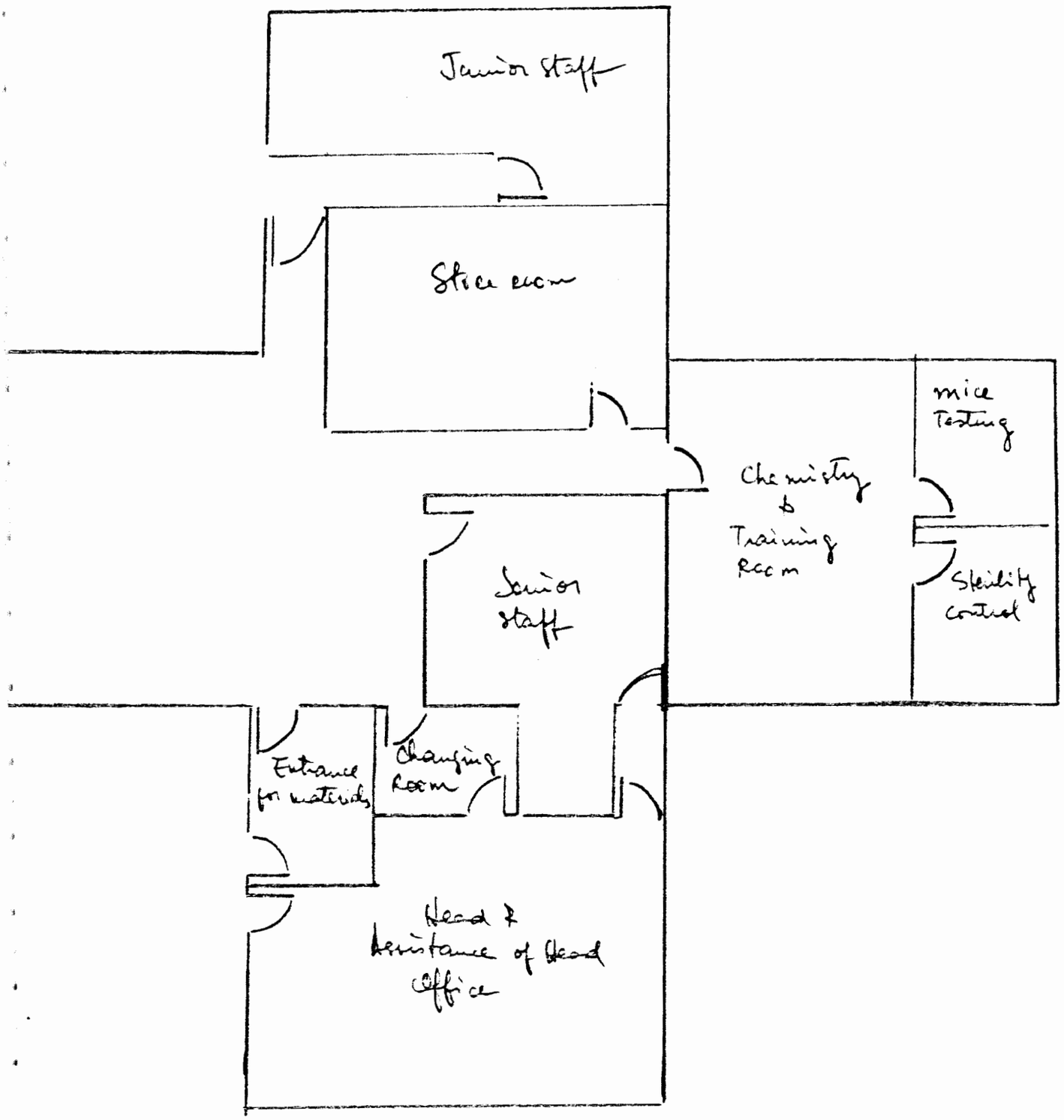
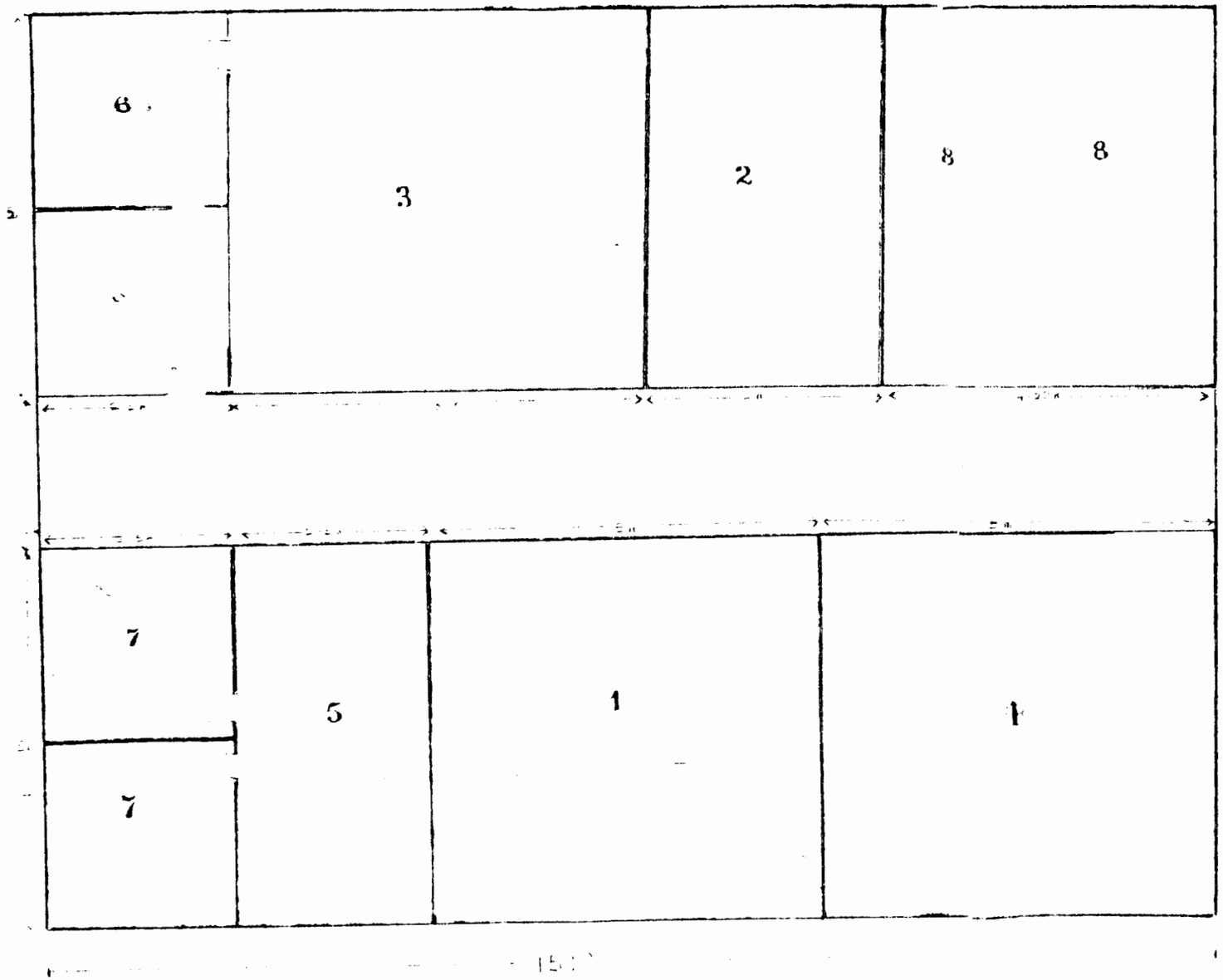
Alternative layout for right wing



ANNEX 9-d

DILUENT LABORATORY YABA



1 WATER PURIFICATION LAB

2 TITRATION LAB

3 DILUENT FILLING LAB

4 STERILIZATION AND DRY WARM CHAMBER

5 DILUENT COMPETENCE ROOM

6

7

8

Annex 9-e

Current Facilities